Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a (SGB V)
Quizartinib (acute myeloid leukaemia, FLT3-ITD-positive)

of 1 August 2024

At its session on 1 August 2024, the Federal Joint Committee (G-BA) resolved to amend the Pharmaceuticals Directive (AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended by the publication of the resolution of D Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

I. Annex XII shall be amended in alphabetical order to include the active ingredient Quizartinib as follows:

Quizartinib

Resolution of: 1 August 2024
Entry into force on: 1 August 2024
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 6 November 2023):

VANFLYTA is indicated in combination with standard cytarabine and anthracycline induction and standard cytarabine consolidation chemotherapy, followed by VANFLYTA single-agent maintenance therapy for adult patients with newly diagnosed acute myeloid leukaemia (AML) that is FLT3-ITD positive.

Therapeutic indication of the resolution (resolution of 1 August 2024):

See therapeutic indication according to marketing authorisation.

1. Additional benefit of the medicinal product in relation to the appropriate comparator therapy

Adults with newly diagnosed acute myeloid leukaemia (AML) that is FLT3-ITD positive

Appropriate comparator therapy:

- An induction chemotherapy:

  Cytarabine in combination with daunorubicin and midostaurin

- Followed by consolidation therapy:

  A patient-individual therapy under selection of chemotherapy (cytarabine in combination with midostaurin) and allogeneic stem cell transplantation, depending in particular on the subtype of AML, the general condition and comorbidity of the patients.

- Followed by maintenance treatment:

  A patient-individual therapy under selection of:

  - azacitidine (only for subjects who are unsuitable for allogeneic stem cell transplantation)
  - midostaurin (only for subjects who are unsuitable for allogeneic stem cell transplantation)
  - sorafenib (only for subjects after allogeneic stem cell transplantation)

  taking into account induction and consolidation therapy

Extent and probability of the additional benefit of quizartinib in combination with standard cytarabine and anthracycline induction and standard cytarabine consolidation chemotherapy, followed by quizartinib monotherapy for maintenance treatment versus the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

Adults with newly diagnosed acute myeloid leukaemia (AML) that is FLT3-ITD positive

An additional benefit is not proven.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	There are no assessable data.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	n.a.	There are no assessable data.
Explanations: ↑: statistically significant and relevant positive effect with low/unclear reliability of data ↓: statistically significant and relevant negative effect with low/unclear reliability of data ↑↑: statistically significant and relevant positive effect with high reliability of data ↓↓: statistically significant and relevant negative effect with high reliability of data ↔: no statistically significant or relevant difference ∅: No data available. n.a.: not assessable		

2. Number of patients or demarcation of patient groups eligible for treatment

Adults with newly diagnosed acute myeloid leukaemia (AML) that is FLT3-ITD positive

Approx. 260 to 820 patients

3. Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Vanflyta (active ingredient: quizartinib) agreed upon in the context of the marketing authorisation at the following publicly accessible link (last access: 23 July 2024):

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A24-16) unless otherwise indicated.

https://www.ema.europa.eu/en/documents/overview/vanflyta-epar-medicine-overview_en.pdf

Treatment with quizartinib should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with acute myeloid leukaemia.

In accordance with the European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients.

The training material contains, in particular, information and warnings on prolongation of the QTc interval.

FLT3 detection

Before taking quizartinib, AML patients must have confirmation of FLT3-ITD positive AML using a CE-marked in vitro diagnostic (IVD) medical device with the corresponding intended purpose. If a CE-marked IVD is not available, confirmation of FLT3-ITD positive AML should be assessed by an alternate validated test.

4. Treatment costs

Annual treatment costs[2]:

Adults with newly diagnosed acute myeloid leukaemia (AML) that is FLT3-ITD positive

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Induction therapy (quizartinib + cytarabine + daunorubicin or idarubicin)	
Quizartinib	€ 8,694.51 - € 17,389.02
Cytarabine	€ 90.18 - € 270.54
Daunorubicin	€ 555.00 - € 1,110.00
Idarubicin	€ 1,113.78 - € 2,227.56
Consolidation therapy (quizartinib + cytarabine)	
Quizartinib	€ 8,694.51 - € 34,778.04
Cytarabine	€ 1,319.52 - € 5,278.08
Total	*€ 10,014.03 - € 40,056.12*
Maintenance treatment (quizartinib monotherapy)	
Quizartinib	€ 117,619.30 - € 186,952.78
Total costs of induction, consolidation and maintenance treatment[3]	
*I: Quizartinib + cytarabine + **daunorubicin*** *K: Quizartinib + cytarabine*	*€ 136,973.02- € 245,778.46*

[2] Only the costs for the first year of treatment are presented.

[3] In patients undergoing haematopoietic stem cell transplantation (HSCT), quizartinib should be discontinued 7 days prior to the conditioning regimen for HSCT. The total costs are therefore different for these patients.

Designation of the therapy	Annual treatment costs/ patient
E: Quizartinib	
*I: Quizartinib + cytarabine + **idarubicin*** *K: Quizartinib + cytarabine* *E: Quizartinib*	*€ 137,531.80- € 246,896.02*
Appropriate comparator therapy:	
Induction therapy	
Cytarabine + daunorubicin + midostaurin	
Cytarabine	€ 135.27 - € 270.54
Daunorubicin	€ 666.00- € 1,332.00
Midostaurin	€ 7,539.88- € 15,079.76
Total	*€ 8,313.25- € 16,626.50*
Consolidation therapy	
Cytarabine + midostaurin	
Cytarabine	€ 5,278.08
Midostaurin	€ 30,159.52
High-dose chemotherapy with allogeneic stem cell transplantation (alloSCT)	
alloSCT	€ 65,407.91 – € 71,031.36
Maintenance treatment	
Oral azacitidine	
Azacitidine	€ 125,651.79- € 140,730.00
Sorafenib	
Sorafenib	€ 2,440.10- € 2,741.97
Midostaurin	
Midostaurin	€ 104,481.19- € 117,406.70
Total costs of the Induction, consolidation and maintenance therapy	
I: Cytarabine + daunorubicin + midostaurin *K: Cytarabine + midostaurin* *Oral azacitidine*	*€ 169,430.54- € 192,849.90*
I: Cytarabine + daunorubicin + midostaurin *K: Cytarabine + midostaurin* *E: **Midostaurin***	*€ 148,259.94- € 169,526.60*
I: Cytarabine + daunorubicin + midostaurin *K: alloSCT* *E: **Sorafenib***	*€ 76,189.16- € 90,455.63*
I: Induction therapy; K: Consolidation therapy; E: Maintenance treatment	

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 July 2024)

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient / year	Costs/ patient / year
Medicinal product to be assessed					
Induction therapy					
Cytarabine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	7	7 - 14	€ 700 - € 1,400
Daunorubicin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	3	3 - 6	€ 300 - € 600
Consolidation therapy					
Cytarabine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	6	6 - 24	€ 600 - € 2,400
Appropriate comparator therapy					
Induction therapy					
Cytarabine + daunorubicin + midostaurin					
Cytarabine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	7	7 - 14	€ 700 - € 1,400
Daunorubicin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	3	3 - 6	€ 300 - € 600
Consolidation therapy					
Cytarabine + midostaurin					
Cytarabine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	6	24	€ 2,400

5. Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

Adults with newly diagnosed acute myeloid leukaemia (AML) that is FLT3-ITD positive

- No medicinal product with new active ingredients that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 1 August 2024.

The justification to this resolution will be published on the website of the G-BA at www.g-ba.de.

Berlin, 1 August 2024

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The Chair

Prof. Hecken